



Joshau Lederberg

Clinical Tests Prove Benefits Of Drugs in Schizophrenia

CLINICAL RESEARCH is very hard to do well, compared to experimental work in the laboratory. Examples of first-class clinical research are so rare that it is a delight to encounter and to write about them, especially when they have important human impact as well as theoretical interest.

Experimental psychiatry has been a particularly discouraging field for scientific observation. Its history is full of fads, there are too few objective tests and we must place heavy reliance on the psychiatrist's subjective evaluation of a patient.

The field is fragmented into contentious schools, each with its own theory of human nature. And undeniably, the psychiatrist's personality plays an important role in the modification of his patient's behavior and in the very criteria of cure. No wonder then that we see dozens of biochemical and socio-psychological theories of schizophrenia, a disease which is now a major concern for public health and private happiness.

THE TREATMENT of schizophrenia would, then, seem to be a very unlikely candidate for rigorous scientific investigation. It is a happy sign of the beginning maturation of scientific psychiatry to see an excellently designed study of drug effects which has an important potential payoff.

This comes from the Psychopharmacology Service Center of the National Institute of Mental Health and was reported in the

Archives of General Psychiatry by Drs. Solomon C. Goldberg and Jonathan O. Cole and their colleagues in a paper entitled, "Prediction of Improvement in Schizophrenia under Four Phenothiazines."

Several different drugs of the phenothiazine group have been developed by research laboratories and drug companies. The best-known is perhaps chlorpromazine; others are fluphanazine, thioridazine and acetophenazine.

Uncontrolled clinical experience with these drugs had suggested that each drug might be particularly efficacious with certain kinds of patients. The NIMH team established a collaborative experiment with a number of hospitals to test this idea. The real distinction of the experiment is that it followed a true double-blind design.

The patients were classified by psychiatric observation before they were assigned AT RANDOM to treatment with one of the drugs or to a placebo — an inert capsule. Furthermore, the medications were coded so that neither the patient nor the attending physician knew which drug was being used until the experiment was finished six weeks later. The patients continued to receive a typical variety of other supportive treatments without any relationship to the encoded medication.

THE IMPROVEMENT under medication did vary with matching the appropriate drug to some previously

observed symptoms. Thus acetophenazine was preferred for paranoid-excited patients; chlorpromazine did best for patients with incoherent speech, and similar differential findings applied to the other drugs.

For a given class of patients, the difference in improvement between the worst compared to the best-matched drug was comparable to the difference between unselected drug and placebo (no drug). Even without further refinements in classifying the patients, the results are therefore of great clinical value. Their theoretical interest in pointing to some of the fundamental issues of the specificity of psychiatric disease is also obvious.

Double-blind methodology is quite essential to reach objective truth in areas where subtle human influences are so important. Unfortunately, this experimental rigor is almost impossible to achieve in certain areas of medicine, sometimes for moral reasons, often for technical ones.

How can a psychotherapist administer a line of treatment without knowing what it is, and without the deepest personal inquiry into the patient's life? We face the same difficulty in other areas where scientific information would be of utmost importance for social policy, for example, in research on methods of education and on differences in academic performance of different colors of children.